SAA (Kobayashi et al, BJH, 2006). Previously, outcomes for alternative donor sources have been inferior secondary to higher rates of graft rejection, GVHD and increased mortality (Bacigalupo et al, Blood, 2000).

Objective: Given the poor outcome of medical therapy for SAA (Bekassy et al, PBC, 2005) and the improvements in HLA matching and outcomes of transplants from alternative donor sources (Maury et al, Haematologica, 2007), we investigated a risk-adapted AlloSCT approach in 22 consecutive patients.

Methods: Patients with <10 transfusions received reduced toxicity conditioning: Cy 60 mg/kg + Flu 180 mg/m^2 + rATG 8 mg/kg (n = 10) or Bu 16 mg/kg + Flu 180 mg/m^2 + Alemtuzumab 54 mg/m^2 (n = 3). 9 patients received myeloablative conditioning: Cy 200 mg/m^2 + Flu 180 mg/m^2 + rATG 8 mg/kg (n = 8) or Bu 16 mg/kg + Mel 135 mg/m^2 + rATG 8 mg/kg (n = 1).

Results: M/F: 14/8, median age: 9.5 years (3-18yrs), median follow-up: 19 months (1-85mos). Stem cell source: Well-MSD BM (9 6/6, 3 5/6); PB (CD34 Selected) MUD (1 10/10, 2 9/10); UCB (4 5/6, 3 4/6). All patients received Tacrolimus and mycophenolate mofetil as AGVHD prophylaxis (Osunkwo/Cairo et al, BBMT, 2004). Median time to neutrophil and platelet engraftment was 14 days (8-32 days) and 32.5 days (11-66 days), respectively. 21 patients engrafted (95% CI: 77.2-99.9); 1 patient had primary graft failure (4.5%). Day +100 mean chimerism was 96.4%, and patients did not differ by intensity of conditioning. Among the 7 patients (31.8%) who developed grade 2-4 GVHD, risk was not associated with conditioning regimen, donor source or HLA match. One-year OS was 71.6% (standard error 9.8%, 95% CI 50.7-92.6%) and an association was not detectable in regards to donor source, HLA disparity or conditioning intensity. Six patients died (27.3%) (multiorgan failure: 3, extensive GVHD: 1, fungal infection: 1, TMA: 1). 3 patients had secondary graft failure (16.6%) and 2 patients required a second transplant secondary to adenovirus and pure red blood cell aplasia. Our data suggest that a risk-adapted approach to AlloSCT from related and alternative donor sources is a feasible strategy for treatment of newly diagnosed pediatric patients with SAA.

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25-HYDROXY VITAMIN D DEFICIENCY IN PEDIATRIC PATIENTS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANT

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Pediatric patients following hematopoietic stem cell transplant (HSCT) are at increased risk for vitamin D deficiency due to lack of sun exposure and sunscreen use, some medications, and dietary insufficiency. We investigated the incidence of 25-OH vitamin D deficiency in pediatric patients following HSCT. The study population included 90 patients (52 male, 38 female). 11 subjects had autologous HSCTs and 79 received allogeneic HSCTs. The median time from transplant was 177 days (range 13-6873 days). 76% of subjects were Caucasian, 8% Hispanic, 7% Asian, 5% African American, and 4% mixed ethnicity. The underlying diseases were ALL (27.8%), AML/MDS (20%), non-malignant hematologic disorder (18.9%), solid tumor (12.3%), immunodeficiency (7.8%), CML (4.4%), lymphoma (4.4%), and other disorder (4.4%). 27.8% of patients received corticosteroids and 51.1% took calcineurin inhibitors at the time of enrollment. At enrollment, 5 patients received multivitamins and 4 patients took vitamin D supplements. The incidence of 25-OH vitamin D insufficiency, defined as a level less than 30 ng/mL, was 87%. 53% of patients were deficient with levels less than 20 ng/mL. The median 25-OH vitamin D level was 18 ng/mL (mean 21.1 ng/mL). Patients with deficiency were prescribed 50,000 IU of ergocalciferol orally once weekly for 6 weeks. 47 patients received supplementation and post-supplementation values were available for 40 patients. 5 patients died prior to repeat testing and levels were missing for 2 patients. Repeat post-supplementation testing revealed a median level of 30 ng/mL. 12.5% (n = 5) of those supplemented remained deficient 20 ng/mL and 47.5% (n = 19) remained insufficient. This study highlights the need to monitor pediatric patients for vitamin D deficiency. A better understanding of the risk factors and appropriate treatment for vitamin D deficiency following HSCT is needed.

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BUSULFAN + FLUDARABINE, AN EFFECTIVE AND LOW TOXIC REGIMEN IN CHILDREN WITH MALIGNANT AND NON-MALIGNANT DISEASES

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Background: Busulfan as myeloablative agent is used in conditioning prior to pediatric HSCT: mainly in combination with cyclophosphomide. We recently found a clear association between busulfan exposure and outcomes (survival/event free survival). However, toxicity leading to morbidity and associated mortality remains a limiting factor. Comparison studies in adults showed a favorable toxicity profile for fludarabine + busulfan (FludBu) compared to the conventional BuCy regimen. In paediatrics, limited data is available regarding this regimen. FludBu was recently introduced to replace the BuCy regimen in our center for myeloid malignancies and all non-malignant indications. We compared the outcomes with our BuCy historic controls.

Methods: Fludarabine was given in 1 hour prior to a 3 hour infusion of once daily busulfan. The target area under the curve (AUC) for Bu was > 74 mg*h/L (in total) in both groups. Busulfan dose targeting, based on therapeutic drug monitoring was performed before the second dose. Primary endpoints were event free survival (EFS) and survival. Secondary endpoints were acute graft-versus-host disease (aGvHD), neutropenic period and the number of erythrocytes and thrombocytes transfusions. A risk factor analysis was performed using univariable and multivariable COX regression.

Results: 13 patients were included in the FludBu group (median follow up median 119 days; range 42-1593) and 44 in the BuCy group (710 days; range 6-1686). The groups were comparable regarding donor source, age, gender, indication for SCT and match-grade. EFS and Survival in FludBu and BuCy was 85% vs 71% (NS) and 92% vs. 73% (NS), respectively. No difference in aGvHD (≥grade 2) was found between the 2 groups. The period of neutropenia was median 12 in the FludBu group compared to 20.5 in the BuCy group (HR 0.38, p = 0.05, CI95% 0.20-0.75). The median number of erythrocytes transfusion was 1 (range 1-13) in the FludBu group and 5 (0-22) in the BuCy group (p = 0.20) and thrombocyte infusions 5 (range 0-33) vs 10 (range 2-44)(p = 0,15).

Conclusions: Busulfan with a total target AUC of >74 mg*h/l in combination fludarabine showed to be an effective and low toxic regimen. Interesting is the significantly shorter neutropenic period and lower number of transfusions (erythrocytes and thrombocytes) needed in the FludBu group in comparison to BuCy. Although a small series, FludBu showed promising results. Further follow up and extension of the series is needed.

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PERI-TRANSPLANT INFECTIONS IN UNRELATED CORD BLOOD TRANSPLANTATION AND THEIR INFLUENCE ON OUTCOME

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Infection in the peri-transplant period is a major cause of morbidity and mortality post-transplant. The nature of peri-transplant infections and their influence on outcome post unrelated cord blood transplant (UCBT) need to be further elucidated.

Methods: We reviewed peri-transplant infections in 81 consecutive UCBT. All culture-documented infections were reviewed starting 3 months pre-transplant through the first 100 days post-transplant. Acute GVHD (aGVHD) II-IV, aGVHD III-IV, chronic GVHD (cGVHD), and event free survival (EFS) were used as endpoints.